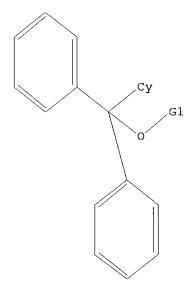
09/288,556

G1 H,Ak

G2 Me,Et,n-Pr,i-Pr,n-Bu,i-Bu,s-Bu,t-Bu,O,N

Structure attributes must be viewed using STN Express query preparation.

=> d 13 L3 HAS NO ANSWERS L3 STR



G1 H,Ak

Structure attributes must be viewed using STN Express query preparation.

=> s 12 sss full FULL SEARCH INITIATED 13:25:49 FILE 'REGISTRY' FULL SCREEN SEARCH COMPLETED - 53916 TO ITERATE

100.0% PROCESSED 53916 ITERATIONS SEARCH TIME: 00.00.01

881 ANSWERS

L4 881 SEA SSS FUL L2

=> s 13 sss full FULL SEARCH INITIATED 13:25:57 FILE 'REGISTRY' FULL SCREEN SEARCH COMPLETED - 249729 TO ITERATE

100.0% PROCESSED 249729 ITERATIONS SEARCH TIME: 00.00.05

56190 ANSWERS

L5 56190 SEA SSS FUL L3

=> file caplus
COST IN U.S. DOLLARS

SINCE FILE TOTAL ENTRY SESSION 315.04 315.25

FULL ESTIMATED COST

FILE 'CAPLUS' ENTERED AT 13:26:15 ON 11 MAR 2004 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

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FILE COVERS 1907 - 11 Mar 2004 VOL 140 ISS 11 FILE LAST UPDATED: 10 Mar 2004 (20040310/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s 14 and T cell proliferation 646 L4

712550 T

1751206 CELL

1560362 CELLS

2348973 CELL

(CELL OR CELLS)

154488 PROLIFERATION

725 PROLIFERATIONS

154947 PROLIFERATION

(PROLIFERATION OR PROLIFERATIONS)

5682 T CELL PROLIFERATION

(T(W)CELL(W)PROLIFERATION)

AB The present invention relates to chemical compds. having inhibitory activity on an intermediate conductance Ca2+-activated potassium channel (IKCa) in T- and B-lymphocytes, and the use of such compds. for the treatment or alleviation of diseases or conditions related to immune dysfunction. The invention also provides a pharmaceutical compns. comprising an effective amount of a IKCa blocker for treatment or alleviation of diseases or conditions related to immune dysfunction. For example, T

cell proliferation was assays 6 days after cells were

stimulated in culture with antigen in the presence of cyclosporin A, or cyclosporin A and clotrimazole, resp. Clotrimazole (10 $\mu M)$ was added 30 min prior to the addition of antigen. The cyclosporin A-mediated

inhibition of T cell proliferation is

shifted leftwards by $\bar{1}0~\mu\text{M}$ clotrimazole, from a 50% inhibition of proliferation at approx. 25 nM cyclosporin A to half-maximal inhibition at 2.5 nM cyclosporin A.

IT 795-36-8, 1,1,1-Triphenylacetone 197526-28-6

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES

(compns. containing potassium channel blockers and immunosuppressants for treatment of immune dysfunction)

RN 795-36-8 CAPLUS

CN 2-Propanone, 1,1,1-triphenyl- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

RN 197526-28-6 CAPLUS

CN 1-Piperidineacetic acid, α , α -diphenyl-, ethyl ester (9CI) (CA INDEX NAME)

REFERENCE COUNT:

THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d 17 1-5 ibib abs hitstr

L7 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

2003:482091 CAPLUS

DOCUMENT NUMBER:

139:180287

TITLE:

Exploring Structure-Activity Relationships of

Transition State Analogues of Human Purine Nucleoside

Phosphorylase

AUTHOR(S):

Evans, Gary B.; Furneaux, Richard H.; Lewandowicz,

Andrzej; Schramm, Vern L.; Tyler, Peter C.

CORPORATE SOURCE:

Carbohydrate Chemistry, Industrial Research Limited,

Lower Hutt, N. Z.

SOURCE:

Journal of Medicinal Chemistry (2003), 46(15),

3412-3423

CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER:

American Chemical Society

DOCUMENT TYPE:

Journal

LANGUAGE:

English CASREACT 139:180287

OTHER SOURCE(S):

The aza-C-nucleosides, Immucillin-H and Immucillin-G, are transition state

analog inhibitors of purine nucleoside phosphorylase, a therapeutic target for the control of **T-cell proliferation**.

Immucillin analogs modified at the 2'-, 3'-, or 5'-positions of the aza sugar moiety or at the 6-, 7-, or 8-positions of the deazapurine, as well as methylene-bridged analogs, have been synthesized and tested for their inhibition of human purine nucleoside phosphorylase. All analogs were poorer inhibitors, which reflects the superior capture of transition state features in the parent immucillins.

IT 402477-42-3P 402477-45-6P 577978-29-1P 577978-30-4P 577978-31-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(exploring structure activity relationships of transition state analogs of human purine nucleoside phosphorylase)

RN 402477-42-3 CAPLUS

CN 1-Pyrrolidinecarboxylic acid, 3,4-dihydroxy-2-[4-methoxy-5-[(phenylmethoxy)methyl]-5H-pyrrolo[3,2-d]pyrimidin-7-yl]-5-[(triphenylmethoxy)methyl]-, 1,1-dimethylethyl ester, (2S,3S,4R,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 402477-45-6 CAPLUS

CN 1-Pyrrolidinecarboxylic acid, 3-hydroxy-4-[(4-methoxyphenyl)methoxy]-5-[4-methoxy-5-[(phenylmethoxy)methyl]-5H-pyrrolo[3,2-d]pyrimidin-7-yl]-2[(triphenylmethoxy)methyl]-, 1,1-dimethylethyl ester, (2R,3R,4S,5S)- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

RN

CN 1-Pyrrolidinecarboxylic acid, 3-hydroxy-5-[4-methoxy-5-[(phenylmethoxy)methyl]-5H-pyrrolo[3,2-d]pyrimidin-7-yl]-4-(2-propenyloxy)-2-[(triphenylmethoxy)methyl]-, 1,1-dimethylethyl ester, (2R,3R,4S,5S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 577978-30-4 CAPLUS

CN 1-Pyrrolidinecarboxylic acid, 3-hydroxy-2-[4-methoxy-5-[(phenylmethoxy)methyl]-5H-pyrrolo[3,2-d]pyrimidin-7-yl]-4-(2-propenyloxy)-5-[(triphenylmethoxy)methyl]-, 1,1-dimethylethyl ester, (2S,3S,4R,5R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 577978-31-5 CAPLUS

CN 1-Pyrrolidinecarboxylic acid, 3-hydroxy-4-[(4-methoxyphenyl)methoxy]-2-[4-methoxy-5-[(phenylmethoxy)methyl]-5H-pyrrolo[3,2-d]pyrimidin-7-yl]-5[(triphenylmethoxy)methyl]-, 1,1-dimethylethyl ester, (2S,3S,4R,5R)- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

REFERENCE COUNT:

THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS 30 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 2 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

2003:376641 CAPLUS

DOCUMENT NUMBER:

138:385438

TITLE:

 ${\tt Preparation} \ \ {\tt of} \ \ {\tt pyridazinylmethanoylphenylhydrazonomalo}$

INVENTOR(S):

nitriles as phosphodiesterase IV inhibitors. Eggenweiler, Hans-Michael; Wolf, Michael; Beier,

Norbert; Schelling, Pierre; Ehring, Thomas

PATENT ASSIGNEE(S):

Merck Patent Gmbh, Germany PCT Int. Appl., 114 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

SOURCE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PA'	PATENT NO. KII					DATE			A	PPLI	CATI	ON N	э.	DATE						
WO	NO 2003039548 A				1	2003	0515	WO 2002-EP11351 20021010												
	W:	AE,	AG,	AL,	AM,	AT,	AU,	AZ,	BA,	BB,	BG,	BR,	BY,	BZ,	CA,	CH,	CN,			
		co,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	ES,	FI,	GB,	GD,	GE,	GH,			
		GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KP,	KR,	ΚZ,	LC,	LK,	LR,			
		LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	ΜZ,	NO,	NZ,	OM,	PH,			
		PL,	PT,	RO,	RU,	SD,	SE,	SG,	SI,	SK,	SL,	ТJ,	TM,	TN,	TR,	TT,	TZ,			
		UA,	UG,	US,	UZ,	VN,	YU,	ZA,	ZM,	ZW,	AM,	AZ,	BY,	KG,	KΖ,	MD,	RU,			
	TJ, TM																			
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		CH,	CY,	CZ,	DE,	DK,	EE,	ES,	FΙ,	FR,	GB,	GR,	ΙE,	IT,	LU,	MC,	NL,			
. ,		PT,	SE,	SK,	TR,	BF,	ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MR,			
		NE,	SN,	TD,	TG															
RIT'	Y APP	LN.	INFO	. :	EP 2001-125455 A 20011105															
ER SO	OURCE	(S):			MARPAT 138:385438															

PRIO

OTHER SOURCE(S):

GΙ

$$R^{1}$$
 $N-N$
 R^{31}
 R^{31}
 R^{4}
 R^{4}

Title compds. [I; R1, R2 = H, OH, OR5, SR5, SOR5, SO2R5, X; R1R2 = OCH2O, OCH2CH2O; R3, R31 = H, R5, OH, OR5, NH2, NHR5, NHCOR5, X, CO2H, CO2R5, CONH2, etc.; R4 = cyano, tetrazolyl; R5 = (fluoro-substituted) A, cycloalkyl, (CH2)nAr; A = (fluoro- and/or chloro-substituted) alkyl, alkenyl; Ar = Ph; n = 0-2; X = F, Cl, Br, iodo], were prepared Thus, [3-(3,4-diethoxyphenyl)-5,6-dihydro-4H-pyridazine-1-yl]-(3-aminophenyl)methanone (preparation given) was stirred with NaNO2 in aqueous HCl for

Ι

1 h at -2° to 0°; malononitrile in H2O was added followed by stirring for 2 h to give a residue which was treated with KOH in MeOH to give 2-[[3-[1-[3-(3,4-diethoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]methanoyl]phenyl]hydrazono]malononitrile K salt. I were said to give a marked reduction of **T cell proliferation**. I are claimed for treatment of osteoporosis, tumors, cachexia, atherosclerosis, rheumatoid arthritis, multiple sclerosis, diabetes mellitus, inflammatory processes, allergies, asthma, autoimmune diseases, myocardial diseases, AIDS, etc.

IT 83799-24-0, Fexofenadine

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (coadministration; preparation of pyridazinylmethanoylphenylhydrazonomalonit riles as phosphodiesterase IV inhibitors)

RN 83799-24-0 CAPLUS

CN Benzeneacetic acid, $4-[1-hydroxy-4-[4-(hydroxydiphenylmethyl)-1-piperidinyl]butyl]-<math>\alpha$, α -dimethyl- (9CI) (CA INDEX NAME)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

2000:824108 CAPLUS

DOCUMENT NUMBER:

134:536

TITLE:

Chemical compounds having potassium channel blocking

activity for the treatment of immune dysfunction

INVENTOR(S):

Jensen, Bo Skaaning; Olesen, Soren Peter;

Christophersen, Palle

PATENT ASSIGNEE(S):

Neurosearch A/S, Den.

SOURCE:

PCT Int. Appl., 45 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 1 PATENT INFORMATION:

PA	TENT	NO.		KIND DATE					A)	PPLI	CATI	ο.	DATE									
WO	2000	A1 20001123				W	20	00-DI		20000512												
	W: AE, AG,			AL,	AM,	ΑT,	AU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	CA,	CH,	CN,	CR,					
		CU,	CZ,	DE,	DK,	DM,	DZ,	EE,	ES,	FI,	GB,	GD,	GE,	GH,	GM,	HR,	HU,					
	ID, IL, LV, MA,			IN,	IS,	JP,	KE,	KG,	KP,	KR,	ΚZ,	LC,	LK,	LR,	LS,	LT,	LU,					
				MD,	MG,	MK,	MN,	MW,	MX,	NO,	NZ,	PL,	PT,	RO,	RU,	SD,	SE,					
	SG, SI,				SL,	ТJ,	TM,	TR,	TT,	TZ,	UA,	UG,	US,	UZ,	VN,	YU,	ZA,					
		ZW,	AM,	ΑZ,	BY,	KG,	KΖ,	MD,	RU,	ТJ,	TM											
	RW:	GH,	GM,	ΚE,	LS,	MW,	SD,	SL,	SZ,	TZ,	UG,	ZW,	AT,	BE,	CH,	CY,	DE,					
		DK,	ES,	FI,	FR,	GB,	GR,	IE,	IT,	LU,	MC,	NL,	PT,	SE,	BF,	ВJ,	CF,					
		CG,	CI,	CM,	GΑ,	GN,	GW,	ML,	MR,	NE,	SN,	TD,	TG									
EP	1181	016		A	1	2002	0227		E.	P 20	00-9	9	20000512									
	R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LI,	LU,	NL,	SE,	MC,	PT,					
	IE, SI, LT, LV, FI, RO																					
US	US 2002065247 A1 20020530										us 2001-986725 /20011109											
PRIORIT		DK 1999-659 A 19990512																				
											WO 2000-DK253 W 20000512											

OTHER SOURCE(S): MARPAT 134:536

AB The present invention relates to chemical compds. having inhibitory activity on an intermediate conductance Ca2+-activated potassium channel (IKCa) in T- and B-lymphocytes, and the use of such compds. for the treatment or alleviation of diseases or conditions related to immune dysfunction. The invention also provides a pharmaceutical compns. comprising an effective amount of a IKCa blocker for treatment or alleviation of diseases or conditions related to immune dysfunction. For example, T cell proliferation was assays 6 days after cells were stimulated in culture with antigen in the presence of cyclosporin A, or cyclosporin A and clotrimazole, resp. Clotrimazole (10 μM) was added 30 min prior to the addition of antigen. The cyclosporin A-mediated inhibition of T cell proliferation is shifted leftwards by 10 μM clotrimazole, from a 50% inhibition of proliferation at approx. 25 nM cyclosporin A to half-maximal inhibition at 2.5 nM cyclosporin A.

IT 6922-89-0, (4-Chlorophenyl-diphenyl)-carbinol
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(compns. containing potassium channel blockers and immunosuppressants for treatment of immune dysfunction)

RN 6922-89-0 CAPLUS

CN Benzenemethanol, 4-chloro- α , α -diphenyl- (9CI) (CA INDEX NAME)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN ACCESSION NUMBER: 1999:344846 CAPLUS

DOCUMENT NUMBER:

131:13987

TITLE:

Chemical compounds having ion channel blocking activity for the treatment of immune dysfunction

INVENTOR(S):

Olesen, Soren-Peter; Jensen, Bo Skaaning; Jorgensen, Tino Dyhring; Strobaek, Dorte; Christophersen, Palle;

Odum, Niels

PATENT ASSIGNEE(S):

Neurosearch A/S, Den. PCT Int. Appl., 47 pp.

SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PA	PATENT NO.			KII	ND	DATE	DATE APPLICATION NO. DATE												
WO	9925347			A	2	1999	0527				98-DI			19981113					
WO	9925347			A.	3	19990729													
	W:	AL,	AM,	ΑT,	AU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	CA,	CH,	CN,	CU,	CZ,	DE,		
		DK,	EE,	ES,	FI,	GB,	GD,	GE,	GH,	GM,	HR,	HU,	ID,	ΙL,	IS,	JP,	ΚE,		
		KG,	ΚP,	KR,	KZ,	LC,	LK,	LR,	LS,	LT,	LU,	LV,	MD,	MG,	MK,	MN,	MW,		
	MX, NO,		NZ,	PL,	PT,	RO,	RU,	SD,	SE,	SG,	SI,	SK,	SL,	TJ,	TM,	TR,			
		TT,	UA,	UG,	US,	UZ,	VN,	YU,	ZW,	AM,	ΑZ,	BY,	KG,	ΚZ,	MD,	RU,	ТJ,	TM	
	RW:	GH,	GM,	ΚE,	LS,	MW,	SD,	SZ,	UG,	ZW,	AT,	BE,	CH,	CY,	DE,	DK,	ES,		
		FI,	FR,	GB,	GR,	ΙE,	IT,	LU,	MC,	NL,	PT,	SE,	BF,	ВJ,	CF,	CG,	CI,		
		CM,	GA,	GN,	GW,	ML,	MR,	NE,	SN,	TD,	ΤG								
AU	9912	245		A1 19990607				A	J 19	99-12	2245		19981113						
EP	1052990			A.	2	2000	1122		E	P 19	98-95	5538	7	1998	1113				
	R:	ΑT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LI,	LU,	ΝL,	SE,	PT,	ΙE,	FI	
US									US 2000-55064										
US	6545	028		B	2	2003	0408												
PRIORITY APPLN. INFO.:									DK 1	997-	1298		Α	1997	1114				
									DK 1	998-	386		Α	1998	0319				
								1	wo 1	998-	DK490	C	W	1998	1113				

OTHER SOURCE(S): MARPAT 131:13987

The present invention relates to chemical compds. having inhibitory activity on an intermediate conductance Ca2+-activated potassium channel (IKCa), and the use of such compds. for the treatment or alleviation of diseases or conditions relating to immune dysfunction. Moreover, the invention relates to a method of screening a chemical compound for inhibitory activity on an intermediate conductance Ca2+ activated potassium channel (IKCa). E.g., clotrimazole and nitrendipine inhibited antigen-induced Tcell proliferation and thus are useful for reduction or inhibition of undesired immunoregulatory actions. From the kinetics of inhibition of Ca2+-activated potassium current, an IC50 value of 153 nM for clotrimazole was calculated

IT 66774-02-5

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(screening of Ca2+-activated potassium channel inhibitors for treatment of immune dysfunction)

RN 66774-02-5 CAPLUS

Benzenemethanol, 2-chloro- α , α -diphenyl- (9CI) (CA INDEX NAME) CN

ANSWER 5 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

1995:102289 CAPLUS

DOCUMENT NUMBER:

122:240203

TITLE:

Synthesis of immunosuppressive neoglycoproteins:

bovine serum albumin coupled with 8-(hydrazinocarbonyl)octyl 4- or 6-0- α -Dmannopyranosyl- α -D-mannopyranoside

AUTHOR(S):

Wada, Kaoru; Chiba, Taku; Takei, Yutaka; Ishihara,

Hideko; Hayashi, Hidetoshi; Onozaki, Kikuo

CORPORATE SOURCE:

Fac. Pharmaceutical Sci., Nagoya City Univ., Nagoya,

467, Japan

SOURCE:

Journal of Carbohydrate Chemistry (1994), 13(7),

941-65

CODEN: JCACDM; ISSN: 0732-8303

DOCUMENT TYPE:

Journal

English

LANGUAGE:

AΒ The title compds. were prepared by standard methods and coupled with bovine serum albumin by the acyl azide method. Antibodies against the mannose dimers were generated and an ELISA was established to measure small amts. of mannose dimers coupled to proteins. The title compds. appeared to inhibit the antigen-specific human T cell

proliferation over 100-fold more efficiently than free mannose dimers.

162129-96-6P IT

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(synthesis of immunosuppressive bovine serum albumin-coupled hydrazinocarbonyloctyl mannopyranosylmannopyranoside)

RN162129-96-6 CAPLUS

Nonanoic acid, $9-[[2,3,4-tri-O-acetyl-6-O-(triphenylmethyl)-\alpha-D-$ CN mannopyranosyl]oxy]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

